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A method of identifying the biological function of a candidate gene, the method comprising the steps of:

- (i) selecting a first candidate gene;
- (ii) providing a first zinc finger protein that binds to a first target site of the first candidate gene and a second zinc finger protein that binds to a target site of a second gene;
- (iii) culturing a first cell under conditions where the first zinc finger protein contacts the first candidate gene and culturing a second cell under conditions where the second zinc finger protein contacts the second candidate gene, wherein the first and the second zinc finger proteins modulate expression of the first and second candidate genes; and
- (iv) assaying for a selected phenotype, thereby identifying whether or not the first candidate gene is associated with the selected phenotype.
- 2. The method of claim 1, further comprising providing a third zinc finger protein that binds to a second target site of the first candidate gene.
- 3. The method of claim 1, further comprising selecting a plurality of candidate genes and providing a plurality of zinc finger proteins that bind to a target site of each candidate gene.
 - 4. The method of claim 1, wherein the second gene is a control gene.
 - 5. The method of claim 1, wherein the first candidate gene is partially encoded by an EST of at least about 200 nucleotides in length.
 - 6. The method of claim 1, wherein the first candidate gene and the second gene are both associated with the selected phenotype.
- 7. The method of claim 1, wherein the first and second cell are the same cell, wherein the cell comprises the first and second candidate genes.
 - The method of claim 1, wherein the first and the second candidate genes are endogenous genes.

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The method of claim 1, wherein expression of the candidate genes is inhibited by at least about 50%.

- 10. The method of claim 1, wherein expression of the candidate genes is activated by at least about 150%.
- 1 11. The method of claim 1, wherein the zinc finger proteins are fusion 2 proteins comprising a regulatory domain.
 - 12. The method of claim 1, wherein expression of the zinc finger proteins is induced by administration of an exogenous agent.
 - 13. The method of claim 11, wherein the zinc finger proteins are fusion proteins comprising at least two regulatory domains.
 - 14. The method of claim 1, wherein the cell is selected from the group consisting of animal cell, a plant cell, a bacterial cell, a protozoal cell, or a fungal cell.
 - 15. The method of claim 14, wherein the cell is a mammalian cell
 - 16. The method of claim 15, wherein the cell is a human cell
 - 1 17. The method of claim 1, wherein the modulation of expression is activation of gene expression that prevents repression of gene expression.
 - 1 18. The method of claim 1, wherein the modulation of expression is inhibition of gene expression that prevents gene activation.
 - 19. The method of claim 11, wherein the regulatory domain is selected from the group consisting of a transcriptional repressor, a methyl transferase, a transcriptional activator, a histone acetyltransferase, and a histone deacetylase.
 - The method of claim 1, wherein the first and second zinc finger proteins are encoded by an expression vector comprising a zinc finger protein nucleic acid operably linked to a promoter, and wherein the method further comprises the step of first administering the expression vector to the cell.

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21. The method of claim 20, wherein expression of the zinc finger proteins is under small molecule control.

- 22. The method of claim 21, wherein expression of the first zinc finger protein and expression of the second zinc finger protein are under different small molecule control, wherein both the first and the second zinc finger protein are fusion proteins comprising a regulatory domain, and wherein the first and the second zinc finger proteins are expressed in the same cell.
- 23. The method of claim 22, wherein both the first and the second zinc finger proteins comprise a regulatory domain that represses gene expression.
 - 24. The method of claim 20, wherein the expression vector is a viral vector.
- 25. The method of claim 24, wherein the expression vector is a retroviral expression vector, an adenoviral expression vector, or an AAV expression vector.
- 26. The method of claim 20, wherein the zinc finger proteins are encoded by a nucleic acid operably linked to an inducible promoter.
- 1 27. The method of claim 1, wherein the cell comprises less than about 1.5x10⁶ copies of each zinc finger protein.
 - The method of claim 1, wherein the target site is upstream of a transcription initiation site of the candidate gene.
 - 29. The method of claim 1, wherein the target site is adjacent to a transcription initiation site of the candidate gene.
- 1 30. The method of claim 1, wherein the target site is adjacent to an RNA polymerase pause site downstream of a transcription initiation site of the candidate gene.
- 1 31. A method of identifying the biological function of a candidate 2 gene, the method comprising the steps of:

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	(i) identifying a plurality of candidate genes;
3	(ii) providing a first zinc finger protein that binds to a first target site of a
4	
5	first candidate gene; (iii) culturing a first cell under conditions where the first zinc finger
6	(iii) culturing a first cell under conditions
7	protein contacts the first candidate gene, wherein the first zinc finger protein modulates
8	expression of the first candidate gene;
9	(iv) determining the expression pattern of the candidate genes and
10	determining whether or not the first candidate gene is associated with the selected
11	havetime; and
12	(v) repeating steps (ii)-(iv) for each candidate gene.
•	The method of claim 31, further comprising providing a second
1	32. The method of claim 31, factors of the first candidate gene.
2	zinc finger protein that binds to a second target say
1	The method of claim 31, wherein at least one of the candidate
1	genes is an EST of at least about 200 nucleotides in length.
2	34. The method of claim 31, wherein at least two candidate genes are
1	
2	
	The method of claim 31, wherein the candidate genes are
1	
2	endogenous genes.
	The method of claim 31, wherein expression of the candidate genes
	2 is inhibited by at least about 50%.
•	wherein expression of the candidate genes
	1 10 1
	2 is activated to at least about 150%
	The method of claim 31, wherein the zinc finger protein is a fusion
	ining a regulatory Homain.
	2 protein comprising a regulatory possible and a significant domain is under
	The method of claim 38, wherein the regulatory domain is under
	2 small molecule control.
	1 40. The method of claim 38, wherein the zinc finger proteins are fusion
	ing at least two regulatory domains.
	2 proteins comprising at least two regularity

the cell is selected from the	
The method of claim 31, wherein the cell is selected from the	
The method of claim 31, wherein 2 group consisting of animal cell, a plant cell, a bacterial cell, a protozoal cell, or a fungal	
2 cell	
wherein the cell is a mammalian cell	
The method of claim 42, wherein the cell is a human cell	
wethod of claim 31, wherein the modulation of expression is	
1 44. The method of claims 37, 2 activation of gene expression that prevents repression of gene expression.	
2 activation of gene expression that page 2	
The method of claim 31, wherein the modulation of expression is	
1 1 45. The second of 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
The method of claim 38, wherein the regulatory domain is selected	
1 46. The method of claim 36, had a methyl transferase, a 2 from the group consisting of a transcriptional repressor, a methyl transferase, a contract transferase, and a histone deacetylase.	
from the group consisting of a transcriptional representation. from the group consisting of a transcriptional representation of a transcriptional activator, a histone acetyltransferase, and a histone deacetylase.	
3 transcriptional activator, a firstone and the sine finger protein is encoded	
The method of claim 31, wherein the zinc finger protein is encoded 1 47. The method of claim 31, wherein the zinc finger protein is encoded	
by an expression vector comprising a zinc finger protein has by an expression vector comprising a zinc finger protein has promoter, and wherein the method further comprises the step of first administering the promoter, and wherein the method further comprises the step of first administering the	
4 expression vesses 48. The method of claim 47, wherein expression of the zinc finger	
protein is under small molecule control.	
2 protein is under small and the protein is under small and th	
1 49. The method of claim 47, which are	
2 vector.	
The method of claim 49, wherein the expression vector is a	
is the recession vector, an adenoviral expression vector, or an AAV oxpression	
yector. The method of claim 47, wherein the zinc finger protein is encoded	
1 51. The method of claim 47, where \	
by a nucleic acid operably linked to an inducible promoter. 2 by a nucleic acid operably linked to an inducible promoter.	
The method of claim 31, wherein the cell comprises less than about	
1 2 1.5x10 ⁶ copies of the zinc finger protein.	
2 1.01	

		The method of claim 31, wherein the target site is upstream of a
	1	
	2	transcription initiation site of the candidate gene.
	1	The method of claim 31, wherein the target site is adjacent to a
	2	transcription initiation site of the candidate gene.
	2	The method of claim 31, wherein the target site is adjacent to an
	1	55. The method of claim 31, wherein the target
	2	RNA polymerase pause site downstream of a transcription initiation site of the candidate
	3	gene.
	.1	56. A method of identifying the biological function of a candidate
	2	gene, the method comprising the steps of:
	3	and the standard gene;
		First zing finger that binds to a first target site of the fine
	4	candidate gene and a second zinc finger that binds to a second target site of the first
mil that man	5	\
Ŧ	6	A cell under conditions where the first zame and
r an an an an an	7	1: He keep and culturing a second cell under conditions
15 15 15 15 15 15 15 15 15 15 15 15 15 1	8	antocte the illst callulate Source
) T	9	The modulate explession of the first
nii nii	10	and the second zinc finger projeins indutate on a selected phenotype, thereby identifying whether or not
	11	the first candidate gene is associated with the selected phenotype.
	12	the first candidate gene is associated with
	1	57. The method of claim 56, further comprising providing a third zinc
	1	that hinds to a target site of a second candidate gene.
	-	The method of claim 56, further comprising selecting a plurality of
		The method of claim 56, further comprising services is 1
		The method of Claim 30, takes 2 candidate genes and providing a plurality of zinc finger proteins that bind to a target site
		3 of each candidate gene.
		that of claim 57 wherein the second candidate gene is a
		\
		2 control gene.
		1 60. The method of claim 56, wherein the first candidate gene is an EST
		2 of at least about 200 nucleotides in length.

The method of claim 57, wherein the first car	ndidate gene and the
The method of claim 37, wherein a	enotype.
2 second candidate gene are both required for causing the second	
The method of claim 56, wherein the first an	d second cell are the
2 same cell.	
1 63. The method of claim 56, wherein the first ca	andidate gene is an
a and agenous gene.	
64 The method of claim 56, wherein expression	n of the first candidate
gene is inhibited by at least about 50%.	
,	on of the first candidate
1 1 1 150%	
gene is activated to at least about 150%.	zinc finger protein is a
The method of claim 56, wherein the first	2
1 2 fusion protein comprising a regulatory domain.	
2 fusion protein company 2 67. The method of claim 66, wherein the region 1	alatory domain is under
The method of Claim 1959,	
1 65. The method of claim 56, wherein expression 2 gene is activated to at least about 150%. 1 66. The method of claim 56, wherein the first 2 fusion protein comprising a regulatory domain. 1 67. The method of claim 66, wherein the regulatory domain. 2 small molecule control.	c finger proteins are fusion
The method of claim 66, wherein the 2111	o import
domains.	
" \ \r c \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	ll is selected from the
1 69. The method of claim 90, where 1	protozoal cell, or a fungal
1 69. The method of claim \$6, wherein the second a plant cell, a bacterial cell, a group consisting of animal cell a plant cell, a bacterial cell, a	
2 221	
wherein the co	ell is a mammalian cell
1 70. The method of claim 33,	
71. The method of claim 71, wherein the c	ell is a human cen
1 71. The method of oldman 7	modulation of expression is
The method of claim 56, wherein the r	a overession
1 72. The method of states 1 2 activation of gene expression that prevents repression of gen	e expression.
2 activation of gene express. 73. The method of claim 56, wherein the	modulation of expression is
The method of claim 50, wherein the	
1 inhibition of gene expression that prevents gene activation.	

The method of claim 66, wherein the regulatory domain is selected	
a the repressor, a methyl transferder, a	
from the group consisting of a transcriptional rep. transcriptional activator, a histone acetyltransferase, and a histone deacetylase.	
3 transcriptional activator, a histone acetyltransferast,	
wherein the first and the second zinc	
l comprising a zinc migor protein	
finger proteins are encoded by an expression vector comprises nucleic acid operably linked to a promoter, and wherein the method further comprises the	
nucleic acid operably linked to a promoter,	
nucleic acid operatory many step of first administering the expression vector to the cell.	
The method of claim 75, wherein expression of the zinc finger	
l molecule control.	
2 proteins is under small molecular	
2 proteins is under the first zinc finger 77. The method of claim 76, wherein expression of the first zinc finger	
The method of claim 70, where 2 Protein and expression of the second zinc finger protein are under different small 2 Protein and expression of the second zinc finger protein are fusion	
protein and expression of the second zinc finger protein are fusion molecule control, wherein both the first and the second zinc finger molecule control, wherein both the first and wherein the first and the second zinc finger	•
a comprising a regulatory domain, and who	
expressed in the same cell. \ / \	
5 proteins are expressed in a 78. The method of claim 77, wherein the first zinc finger protein	
78. The method of claim 77, wherein the first zinc finger protein 1 comprises a regulatory domain that represses gene expression and the second zinc finger 2 comprises a regulatory domain that activates gene expression.	
2 comprises a regulatory domain that represses gene expression.	
2 comprises a regulatory domain that activates gene expression. 3 protein comprises a regulatory domain that activates gene expression.	
athed of claim 75, wherein the expression vector is a vital	
1 79. The method of the state o	
2 vector.	
The method of claim 79, wherein the expression vector is a	
is the approximate vector, an adenoviral expression vector, of all 1911 of	
yector. 81. The method of claim 75, wherein the zinc finger proteins are	
1 81. The method of claim /3, wherein the same of the	
had by a pucleic acid operably linked to all industrial	
of claim 56, wherein the cell comprises less than 5	bout
1 82. The method of class 1	
2 1.5x10 ⁶ copies of each zinc finger protein.	site
2 1.5x10 copies of case 2 1.5x10 copies 2 1.5x	
of a transcription initiation site of the first candidate gent.	
2 is upstream of a transcription \	

	The method of claim 56, wherein the first or the second target site
1	The method of claim 36, wherein the first of the
2	is adjacent to a transcription initiation site of the first candidate gene.
-	The method of claim 56, wherein the first or the second target site
1	85. The method of claim 50, wherein the
2	is adjacent to an RNA polymerase pause site downstream of a transcription initiation site
3	of the first candidate gene.
,	sidentifying the biological function of a candidate
1	\ \ \/
2	gene, the method comprising the steps of:
3	(i) selecting a first candidate gene;
`4	(i) selecting a first callulate sens, (ii) providing a first zinc finger protein that binds to a first target site of the
5	
	wing a first cell under conditions where the first cells
6	and the contacts the first candidate gene, wherein the first zinc imger protection
7	a.t. Ct. andidate gene: allu \
8	modulate expression of the first candidate gent, and the first candidat
9	(iv) assaying for a selected phonotype.
10	the first candidate gene is associated with the selected phenotype.
10 10	
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